



SEQUENCE LISTING

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<120> CONJUGATES COMPRISING HUMAN IL-18 AND
SUBSTITUTION MUTANTS THEREOF

<130> PU60053

<140> 10/823,964
<141> 2004-04-14

<150> 60/462,947
<151> 2003-04-15

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 157
<212> PRT
<213> Homo sapiens

<400> 1
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Glu Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 2
<211> 157

<212> PRT
<213> Mus musculus

<400> 2
Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg Asn Ile Asn
1 5 10 15
Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe Glu Asp Met
20 25 30
Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg Leu Ile Ile
35 40 45
Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly Leu Ala Val Thr Leu Ser
50 55 60
Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn Lys Ile Ile
65 70 75 80
Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp Ile Gln Ser
85 90 95
Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn Lys Met Glu
100 105 110
Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys Gln Lys Glu
115 120 125
Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu Asn Gly Asp
130 135 140
Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser
145 150 155

<210> 3
<211> 203
<212> PRT
<213> Homo sapiens

<400> 3
Met His His His His His His Thr Arg Gly Met Ala Ala Glu Pro Val
1 5 10 15
Glu Asp Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr
20 25 30
Leu Tyr Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe
35 40 45
Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln
50 55 60
Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr
65 70 75 80
Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ser
85 90 95
Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val
100 105 110
Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser
115 120 125
Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp
130 135 140
Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln
145 150 155 160
Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu
165 170 175
Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp
180 185 190

Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
195 200

<210> 4
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18 sequence has been replaced with Serine.

<400> 4
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 5
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Asparagine at position 78 has been replaced with Cysteine.

<400> 5
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60

Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Cys Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 6
<211> 157
<212> PRT
<213> Homo sapiens

<220>

<223> Whereby the Cysteine at position 38 of thi human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Glutamic acid at position 121 has been replaced with Cysteine.

<400> 6
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Tyr Cys Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 7
<211> 157
<212> PRT
<213> Homo sapeins

<220>

<223> Whereby the Cysteine at position 38 of this human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Leucine at position 144

has been replaced with Cysteine.

<400> 7
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Cys
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 8
<211> 157
<212> PRT
<213> Homo sapiens

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and Aspartic acid at position 157 has been replaced with Cysteine.

<400> 8
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Cys
145 150 155

<210> 9
<211> 157
<212> PRT
<213> Homo sapeins

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Leucine at position 144 has been replaced with Cysteine.

<400> 9

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5				10				15			
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
				20				25				30			
Met	Thr	Asp	Ser	Asp	Ser	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
	35					40					45				
Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile
	50					55				60					
Ser	Val	Lys	Ser	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile
	65					70				75			80		
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
		85					90					95			
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
		100					105				110				
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
	115						120				125				
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Cys
	130					135				140					
Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Asp			
	145					150				155					

<210> 10

<211> 157
<212> PRT
<213> Homo sapiens

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Aspartic acid at position 157 has been replaced with Cysteine.

<400> 10

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5				10				15			
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
				20				25				30			
Met	Thr	Asp	Ser	Asp	Ser	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
		35					40				45				

Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Ser Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Cys
145 150 155

<210> 11

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 11

Tyr Phe Gly Lys

1

<210> 12

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 12

Leu Glu Ser Lys

1

<210> 13

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 13

Leu Ser Val Ile Arg
1 5

<210> 14
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 14
Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu
1 5 10 15
Phe Glu Asp Met Thr Asp Ser Asp Cys Arg
20 25

<210> 15
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 15
Asp Asn Ala Pro Arg
1 5

<210> 16
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 16
Thr Ile Phe Ile Ile Ser Met Tyr Lys
1 5

<210> 17
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 17
Asp Ser Gln Pro Arg
1 5

<210> 18
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 18
Gly Met Ala Val Thr Ile Ser Val Lys
1 5

<210> 19
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 19
Ile Ser Thr Leu Ser Cys Glu Asn Lys
1 5

<210> 20
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 20
Ile Ile Ser Phe Lys
1 5

<210> 21
<211> 9
<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 21
Glu Met Asn Pro Pro Asp Asn Ile Lys
1 5

<210> 22
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 22
Ser Asp Ile Ile Phe Phe Gln Arg
1 5

<210> 23
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 23
Ser Val Pro Gly His Asp Asn Lys
1 5

<210> 24
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 24
Met Gln Phe Glu Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
1 5 10 15
Lys

<210> 25
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 25
Asp Leu Phe Lys
1

<210> 26
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 26
Leu Ile Leu Lys
1

<210> 27
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 27
Glu Asp Glu Leu Gly Asp Arg
1 5

<210> 28
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 28

Ser Ile Met Phe Thr Val Gln Asn Glu Asp
1 5 10